Appl. No. : 09/804,457
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AMENDMENTS TO THE CLAIMS

1. (Presently Amended): A method of characterizing the biological activity of a candidate compound comprising:

exposing one or more cells to said compound;

repetitively exposing said one or more cells to one or more electric fields so as to effect a controlled change in transmembrane potential of said one or more cells without using a patch clamp; and

monitoring, without using a patch clamp, changes in the transmembrane potential of said one or more cells to characterize the biological activity of said compound.

2. (Original): The method of Claim 1, wherein said monitoring comprises detecting fluorescence emission from an area of observation containing said one or more cells.

3. (Original): The method of Claim 1, wherein said electric fields are biphasic.

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4. (Original): The method of Claim 3, additionally comprising limiting spatial variation in electric field intensity so as to minimize irreversible cell electroporation.

5. (Original): The method of Claim 1, wherein one or more electrical fields cause an ion channel of interest to cycle between different voltage dependent states.

6. (Original): The method of Claim 5, wherein said one or more electrical fields cause an ion channel of interest to open.

7. (Original): The method of Claim 5, wherein said one or more electrical fields cause an ion channel of interest to be released from inactivation.

8. (Original): The method of Claim 1, wherein said one or more cells comprise a voltage sensor selected from the group consisting of a FRET based voltage sensor, an electrochromic transmembrane potential dye, a transmembrane potential redistribution dye, an ion sensitive fluorescent or luminescent molecule and a radioactive ion.

9. (Original): The method of Claim 1, wherein said one or more cells comprise a voltage regulated ion channel.

10. (Original): The method of Claim 9, wherein said voltage regulated ion channel is selected from the group consisting of a potassium channel, a calcium chnanel, a chloride channel and a sodium channel.

11. (Original): The method of Claim 1, wherein said electric field exhibits limited spatial variation in intensity in the area of observation of less than about 25% from a mean intensity in that area.

12. (Original): The method of Claim 11, wherein said one or more electrical fields varies over an area of observation by no more than about 15 % from the mean electrical field at any one time.

13. (Original): The method of Claim 12, wherein said one or more electrical fields varies over an area of observation by no more than about 5 % from the mean electrical field at any one time.

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14. (Original): The method of Claim 1, wherein said one or more electrical fields comprises stimulation with either a square wave-form, a sinusoidal wave-form or a saw tooth wave-form.

15. (Original): The method of Claim 1, wherein said one or more electrical fields have an amplitude within the range of about 10 V/cm to about 100 V/cm.

16. (Original): The method of Claim 15, wherein said one or more electrical fields have an amplitude within the range of about 20 V/cm to about 80 V/cm.

17. (Original): The method of Claim 1, wherein said one or more electrical fields are repeated at a frequency of stimulation that is greater than or equal to the reciprocal of the transmembrane time constant of said one or more cells.

18. (Original): The method of Claim 1, wherein said one or more electrical fields are repeated at a frequency of stimulation within the range of zero to 1kHz.

19. (Original): The method of Claim 1, wherein said one or more electrical fields have a pulse duration within the range of about 100 microseconds to about 20 milliseconds.

20. (Original): The method of Claim 1, wherein said transmembrane potential is developed across the plasma membrane of said one or more cells.

21. (Presently Amended): A method of assaying the biochemical activity of a compound against a target ion channel comprising:

selecting a cell line having a normal resting transmembrane potential corresponding to a selected voltage dependent state of said target ion channel;

expressing said target ion channel in a population of cells of said selected cell line;

exposing said population of cells to said compound;

repetitively exposing said population of cells to one or more electric fields so as to effect a controlled change in transmembrane potential of said ~~one or more~~ population of cells; and

monitoring changes in the transmembrane potential of said ~~one or more~~ population of cells to characterize the biochemical activity of said compound.

22. (Original): The method of Claim 21, wherein said target ion channel is exogenously expressed in the cell line.

23. (Original): The method of Claim 21, wherein said cell line is transfected with nucleic acid encoding said target ion channel.

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24. (Presently Amended): The method of Claim 23, wherein said cell line expresses ~~insignificant levels of other ion channels~~ substantially only said target ion channel.

25. (Original): The method of Claim 24, wherein said cell line is selected from the group consisting of CHL, LTK(-), and CHO-K1.

26. (Original): The method of Claim 21 wherein said target ion channel is a sodium channel, and wherein said population of cells is selected from the group consisting of CHL cells, LTK(-) cells, and CHO-K1 cells.

27. (Original): The method of Claim 21 wherein said target ion channel is a sodium channel, and wherein said population of cells is selected from the group consisting of HEK-293 cells, RBL cells, F11 cells, and HL5 cells.

28. (Original): The method of Claim 21 wherein said target ion channel is a potassium channel, and wherein said population of cells is selected from the group consisting of CHL cells, LTK(-) cells, and CHO-K1 cells.

29. (Original): The method of Claim 21 wherein said target ion channel is a calcium channel, and wherein said population of cells is selected from the group consisting of CHL cells, LTK(-) cells, and CHO-K1 c lls.